

EXHIBIT B

**UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION**

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE
THIS DOCUMENT RELATES TO: <i>Wave 11 Cases</i>	

**RICHARD WASSERMAN, MD, FACOG, FPMRS, GENERAL REPORT REGARDING
TVT, TVT-EXACT, TVT-OBTURATOR, AND TVT-ABBREVO MID-URETHRAL
SLINGS**

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**RICHARD WASSERMAN, MD, FACOG, FPMRS
GENERAL REPORT REGARDING TVT, TVT-EXACT, TVT-OBTURATOR, AND
TVT-ABBREVO MID-URETHRAL SLINGS**

Background:

Richard Wasserman MD FACOG FPMRS

I have been asked to set forth my opinions regarding the safety and efficacy of Ethicon's TVT, TVT-Exact, TVT-Obturator ("TVT-O"), and TVT-Abbrevio mid-urethral slings—each of which I have used in my practice.

Currently I am an employed Urogynecologist and pelvic reconstructive surgeon at Women's Cancer Care of Nevada. I am a private practice urogynecologist with a group that specializes in pelvic surgery. I completed medical school at The Chicago Medical School. I did my internship at The Ohio State University in obstetrics and gynecology. I completed my residency at Dartmouth Medical Center in obstetrics and gynecology. I am board certified in Obstetrics and gynecology and a Fellow in the American Board of Obstetrics and Gynecology (FACOG). I pursued advanced fellowship training in Female Pelvic Medicine and Reconstructive Surgery at Scott and White Medical Center. I am board certified in Female Pelvic Medicine and Reconstructive Surgery (FPMRS). I am a member of the American Urogynecology Society (AUGS).

Since fellowship I have been continuously employed as a pelvic surgeon for the past 12 years. The focus of my practice has been urinary incontinence and pelvic organ prolapse. My practice involves surgical and non-surgical treatment for these conditions. I attend annual continuing medical education meetings and read pelvic medicine journals to stay current. I have treated many patients for urinary incontinence and have implanted many midurethral slings including the TVT, TVT-Exact, TVT-Abbrevio and TVT-O. I was trained on the Burch procedure and on retropubic and trans-obturator slings. I have performed thousands of retropubic mid-urethral sling procedures over the past 13 years, including both TVT and TVT-Exact implant procedure. I have performed hundreds of trans-obturator mid-urethral sling procedures, including both TVT-O and TVT-Abbrevio implant procedures. I continue to use both retropubic and trans-obturator mid-urethral slings in my current practice to treat my patients' stress urinary incontinence. I chose to use Ethicon's TVT, TVT-Exact, TVT-O, and TVT-Abbrevio devices to treat my patients' stress urinary incontinence because of excellent patient satisfaction with minimal complications and because of the wealth of data supporting the devices' safety and efficacy.

I am being compensated \$400 per hour for records review, report preparation, and attorney conferences in this case, \$600 per hour for depositions, \$2,500 per half day of courtroom testimony, \$5,000 for a full day of courtroom testimony, and \$200 per hour for travel or waiting time related to this case.

Stress Urinary Incontinence and Its Traditional Surgical Treatment Options

Stress urinary incontinence is a problem that significantly adversely affects the lives of millions of women in the United States and worldwide. The prevalence of stress urinary incontinence ranges from 29%–75%, with a mean of 48%.¹ The total cost of urinary incontinence in the

¹ Wood LN, and Anger JT, Urinary incontinence in women. BMJ. 2014;349:g4531.

United States is estimated to be as high as \$32 billion per year.² It can be embarrassing for those suffering from it and lead to avoidance of or withdrawal from social situations.

Surgical treatment of stress urinary incontinence is the most clinically effective treatment for this condition. Before mid-urethral sling procedures existed, surgeons treated stress urinary incontinence with proximal or “bladder neck” slings using autologous fascia or urethral suspensions such as the Raz and Stamey procedures, or retropubic urethropexy procedures such as the Burch colposuspension or the Marshall-Marchetti-Krantz (“MMK”) procedure. Each of these procedures carries significant intra-operative risks including hematoma formation, injury to bladder, bowel, nerves, vessels, or other adjacent structures, and surgical hemorrhage. These procedures also carried post-operative risks such as urinary retention, de novo or worsening over-active bladder, dyspareunia, failure of the procedure, erosion, chronic pain, and re-operation for complications or due to failure of the procedure.

Demirci and colleagues published a study analyzing outcomes in 220 women undergoing the Burch colposuspension. At 1.5 years the cure rate was 87.7%, and at 4.5 years it was 77.4%. The percentage of symptom-free patients declined from 83.9% at 3 years to 68% at 6 years.³ Kjølhede published a study of the long-term efficacy of the Burch procedure with a median 14 years of follow-up. Subjectively significant urinary incontinence was experienced by 56% of the questionnaire responders, with only 19% reporting no incontinence episodes.⁴ Alcalay and colleagues reported in 1995 that “[c]ure of incontinence following Burch colposuspension is time-dependent, with a decline for 10-12 years when a plateau of 69% is reached.”⁵

The New England Journal of Medicine published in 2007 a landmark multi-center, randomized clinical trial comparing the autologous fascial sling procedure and Burch procedure—the SISTER trial. The study involved 655 women randomly assigned to undergo one of the two procedures. The authors found that success rates at 24 months were 66% for the autologous sling procedure and 49% for the Burch procedure. The fascial sling patients lost an average of 229 ml of blood and had operative times of 136 minutes, on average. The Burch patients lost an average of 238 ml of blood and had operative times of 138 minutes. Serious adverse events in connection with the Burch procedures included ureteral injury, ureterovaginal fistula, incidental vaginotomy, incidental cystotomy, erosion of suture into the bladder, recurrent cystitis, pyelonephritis, catheter complications, bleeding, and wound complications requiring surgical intervention. In the autologous fascial sling group, complications included incidental cystotomy, recurrent cystitis, pyelonephritis, catheter complications, voiding dysfunction leading to surgical revision, pelvic pain, bleeding, wound complications requiring surgical intervention, respiratory distress requiring intubation, and laryngospasm requiring intubation.⁶ Continence rates in the Burch

² Wood LN, and Anger JT, Urinary incontinence in women. *BMJ*. 2014;349:g4531.

³ Demirci F, et al., Long-Term Results of Burch Colposuspension. *Gynecol Obstet Invest* 2001;51:243-247.

⁴ Kjølhede P, Long-term efficacy of Burch colposuspension: a 14-year follow-up study. *Acta Obstet Gynecol Scand* 2005;84:767-72.

⁵ Alcalay M, et al., Burch colposuspension: a 10-20 year follow up. *Br J Obstet Gynaecol*. 1995 Sep;102(9):740-5.

⁶ Albo ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence. *N Engl J Med*. 2007;356(21):2143-55.

patients decreased at 5 years to 24.1% and at 7 years to 13% and to 30.8% at 5 years and 27% at 7 years in the autologous fascial sling group.⁷

These traditional procedures had significant peri-operative morbidity and, as discussed above, the long-term results were less than optimal. That led to the development of a new surgical treatment for female stress urinary incontinence—the polypropylene mesh mid-urethral sling.

The TVT, TVT-O, TVT-Abbrevio, and TVT-Exact Devices

The TVT, TVT-O, TVT-Abbrevio, and TVT-Exact Devices are mid-urethral slings made of macroporous, lightweight, Prolene polypropylene mesh. They are made of the same Prolene polypropylene suture material that was first developed in the 1960s and approved by the FDA as “safe and effective” in 1969 for its intended uses in the human body.⁸

The Prolene mesh in each of the devices is 1.1 cm wide. The pore size of the mesh is approximately 1.3 mm, and the weight is 100 g/m².⁹ Because the pore size is greater than 75 microns, it is considered Type I mesh. Amid notes that Type I meshes admit macrophages, fibroblasts, blood vessels, and collagen fibers into the pores.¹⁰ The mesh is constructed of knitted filaments, and is a monofilament mesh.

The TVT device was the first of these devices, and its development can be traced back to 1986, with researchers first implanting Mersilene tape first in animals and eventually in humans. It stemmed from the discovery that a hemostat applied at the level of the mid-urethra controlled urine loss with coughing. A Professor of Pathology at the University of Western Australia was consulted to develop and test the surgical methodology and the Mersilene tape for safety, efficacy, and transferability to humans. Testing in humans began in the late 1980s. The human testing involving a removable Mersilene tape led to what was dubbed the integral theory—that loose ligaments caused both stress and urge incontinence but for different reasons: inactivation of urethral forces for USI and activation of the micturition reflex prematurely for urge incontinence. The researchers ultimately concluded that a permanent tape was required and that the erosion rate of Mersilene was too high. Polypropylene was ultimately determined to be the ideal material for use in the slings.¹¹ Dr. Ulmsten is credited with the invention of the TVT device, which has become the most commonly performed procedure for female SUI.¹²

The TVT and TVT-Exact Devices are retropubic mid-urethral slings, while the TVT-O and TVT-Abbrevio are trans-obturator slings. They are implanted using trocars that are attached to

⁷ Brubaker L, et al., 5-Year Continence Rates, Satisfaction and Adverse Events of Burch Urethropexy and Fascial Sling Surgery for Urinary Incontinence. *J Urol.* 2012 Apr;187(4):1324-30; Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. *J. Urol.* 2012 Aug;188:485-89.

⁸ Reynaldo Librojo Declaration at ¶¶ 3-9.

⁹ Moalli PA, et al., Tensile properties of five commonly used mid-urethral slings relative to the TVT. *Int Urogynecol J.* 2008;19:655-663.

¹⁰ Amid PK, Classification of biomaterials and their related complications in abdominal wall hernia surgery. *Hernia* 1997;1:15-21.

¹¹ Petros P, Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond. *Int Urogynecol J.* 2015 Apr;26(4):471-6.

¹² Cox A, et al., Surgical management of female SUI: is there a gold standard? *Nat. Rev. Urol.* 2013;10:78-89.

the mesh—curved trocars for the retropubic slings and helical trocars for the trans-obturator slings. The mesh attached to the trocars and covered with sheaths that aid in placement of the mesh.

The TVT device can be performed with a “bottom-up” approach or a “top-down” approach—the latter performed with abdominal guides.

The TVT-O device consists of a Prolene polypropylene mesh graft measuring 1.1 x 45 cm covered with a plastic sheath and attached to two stainless steel helical passers. The device includes an Atraumatic Winged Guide—a stainless steel accessory instrument that aids in passage of the helical passers through the dissection tract. It was developed in an attempt to minimize the risk of urinary tract injuries associated with retropubic and outside-in trans-obturator midurethral slings.¹³ Jean de Leval published a study in 2003 involving what at the time was a novel surgical treatment of a trans-obturator mid-urethral sling that was implanted not in a lateral-to-medial (“outside-in”) technique, but rather a medial-to-lateral (“inside-out”) technique. De Leval concluded that the technique was feasible, accurate, and quick, and had the positive attributes of avoiding damage to the urethra and bladder due to the trans-obturator route of implantation.¹⁴ This followed earlier studies involving trans-obturator sling implantation by Delorme and others.¹⁵ Ethicon personnel began working with Dr. de Leval in 2002 on what became the TVT-O device, and it was launched in 2004.¹⁶

The TVT-Abbrevio mesh is 1.1 cm x 12 cm and is held between two Helical Passer Sheaths. There is a Placement Loop with an attached polypropylene button in the center of the mesh that assists the surgeon with ensuring a symmetrical placement of the mesh. The TVT-Abbrevio includes an Atraumatic Winged Guide—a stainless steel accessory instrument that facilitates consistent passage of the mesh implant through the dissection tract. Both the TVT-O and TVT-Abbrevio procedures are “inside-out” procedures, meaning they involve a medial-to-lateral implant trajectory rather than a lateral-to-medial “outside-in” trajectory. Dr. Jean de Leval and colleagues published in 2011 an anatomic study comparing a TVT-O sling trajectory with that of a modified sling that was shortened to 12 cm and had a reduced dissection.¹⁷ The authors concluded that the modified device/procedure—what became the TVT-Abbrevio device/procedure—traversed fewer muscular structures than the full-length TVT-O while still consistently anchoring in the obturator membrane at a safe distance from the obturator canal.¹⁸ De Leval and Waltregny developed the TVT-Abbrevio with the goal of reducing the incidence of post-operative groin pain and the theoretical risk of obturator nerve injury. The TVT-Abbrevio was introduced in 2010.

¹³ Waltregny D and de Leval J, New Surgical Technique for Treatment of Stress Urinary Incontinence. TVT-ABBREVO: From Development to Clinical Experience. Surg Technol Int. 2012 Dec;22:149-57.

¹⁴ De Leval J, Novel Surgical Technique for the Treatment of Female Stress Urinary Incontinence: Transobturator Vaginal Tape Inside-Out. Eur Urol 2003;44:724-30.

¹⁵ Delorme E, Transobturator urethral suspension: mini-invasive procedure in the treatment of stress urinary incontinence in women. Prog Urol 2001;11:1306-13.

¹⁶ History of TVT-O. ETH.MESH.03932909-11.

¹⁷ Hinoul P, et al. An anatomic comparison of the original versus a modified inside-out transobturator procedure. Int Urogynecol J. 2011 Aug;22(8):997-1004).

¹⁸ Waltregny D and de Leval J, New Surgical Technique for Treatment of Stress Urinary Incontinence. TVT-ABBREVO: From Development to Clinical Experience. Surg Technol Int. 2012 Dec;22:149-57.

De Leval and Waltregny also published the results of a prospective randomized controlled trial comparing TVT-O and TVT-Abbrevio outcomes at 1 year and 3 years. At 1-year follow-up, they observed a 91.7% SUI cure rate in the TVT-O cohort and a 90.7% cure rate in the TVT-Abbrevio cohort ($p=0.824$). They also found that on post-operative day 0 and 1, there was less groin pain in the TVT-Abbrevio group and that it was less intense, requiring less analgesics. There was no statistically significant difference in the rate of de novo urge symptoms, and approximately 70% of the patients with pre-operative urgency or urge incontinence experienced disappearance or improvement of those symptoms post-operatively, again with no difference between the groups. Less than 10% of patients in both groups experienced de novo voiding difficulties, and there was no statistically significant difference between the groups. There were no intra-operative complications that occurred. One of the TVT-O patients experienced a vaginal mesh exposure requiring partial tape excision. After post-operative day 0 and 1, the incidence of post-operative groin pain did not significantly differ between the two procedures. At the 12-month visit, approximately 3-4% of patients in each group still reported groin pain, which was not severe. The authors concluded that the modified transobturator procedure was as safe and efficacious as the TVT-O procedure, but with less immediate post-operative groin pain.¹⁹ The TVT-Abbrevio studies show acceptably low rates of complications such as mesh exposure, groin pain, and cure or improvement rates of approximately 80–95%.²⁰

The TVT-Exact device was introduced in 2010. Like the TVT, it consists of a 1.1 x 45 cm Prolene mesh graft that is covered with a plastic sheath and implanted via curved trocars. The TVT-Exact trocars are slightly thinner than those of the TVT device (3mm in the TVT-Exact

¹⁹ De Leval J, et al., The original versus a modified inside-out transobturator procedure: 1-year results of a prospective randomized trial. *Int Urogynecol J.* 2011;22:145-156.

²⁰ Tommaselli GA, et al., Efficacy and safety of the trans-obturator TVT-Abbrevio device in normal weight compared to overweight patients affected by stress urinary incontinence. *Eur J Obstet Gynecol Reprod Biol.* 2016 Feb;197:116-9; Capobianco G, et al., TVT-ABBREVO: efficacy and two years follow-up for the treatment of stress urinary incontinence. *Clin Exp Obstet Gynecol.* 2014;41(4):445-7; Dati S, et al., Single-Incision Minisling (Ajust) vs. Obturator Tension-Free Vaginal Shortened Tape (TVT Abbrevio) in Surgical Management of Female Stress Urinary Incontinence. *Int J Gynecol & Obstet.* 2012;119S3:S70 Poster M432; Dati S, et al., TVT-Abbrevio: When and why? *Tech Coloproctol* 2013;17:136; Kurien A, Narang S, Han HC. TVT Abbrevio Prospective analysis over 22 months in a tertiary care hospital. *Br J Obstet Gynecol.* 2014 Jan;121(2):235–236 EP13.17; Canel V, et al., Postoperative groin pain and success rates following transobturator midurethral sling placement: TVT ABBREVO® system versus TVT™ obturator system. *Int Urogynecol J.* 2015 Oct;26(10):1509-16; Shaw JS, et al., Decreasing transobturator sling groin pain without decreasing efficacy using TVT-Abbrevio. *Int Urogynecol J.* 2015 Sep;26(9):1369-72; Feng S, et al., Three- and twelve-month follow-up outcomes of TVT-EXACT and TVT-ABBREVO for treatment of female stress urinary incontinence: a randomized clinical trial. *World J Urol.* 2018 Mar;36(3):459-65; Kurien A, et al., Tension-free vaginal tape-Abbrevio procedure for female stress urinary incontinence: a prospective analysis over 22 months. *Singapore Med J.* 2017 Jun;58(6):338-342; Riachi L and Provost K. A new minimally invasive treatment option for stress urinary incontinence in women: TVT Abbrevio, a shorter sling with an inside-out transobturator approach. *Surg Technol Int.* 2013 Sep;23:176-80; Utekar T, et al., Studying the newer TVT-O Abbrevio tape in comparison with the standard TVT-O tape for management of stress urinary incontinence. *Eur J Obstet Gynecol Reprod Biol.* 2016;206:e117; Li WL, et al., A comparative study on treating female stress urinary incontinence with TVT-Abbrevio and TVT-Obturator; *Zhonghua Yi Xue Za Zhi.* 2016 Jul 26;96(28):2238-40; Melendez Munoz J, et al., MiniArc vs TVT Abbrevio Midurethral Sling in Women with Stress Urinary Incontinence – an RCT – 6 and 12 month follow up. 2017; ICS Abs 718 <https://www.ics.org/2017/abstract/718>; Sun Y, et al., The Efficiency and Safety of Tension-Free Vaginal Tape (TVT) Abbrevio Procedure Versus TVT Exact in the Normal Weight and Overweight Patients Affected by Stress Urinary Incontinence. *Urology.* 2017 Dec;110:63-69.

versus 5mm in the TVT). The TVT-Exact was introduced in 2010. The studies pertaining specifically to the TVT-Exact support the safety and efficacy of the device.²¹

The TVT and TVT-O devices are available in mechanically cut or laser-cut mesh, while the TVT-Abbrevio and TVT-Exact are available only with laser-cut mesh. The Prolene polypropylene used in all of the devices is the same material and has the same pore size and weight.

In 2002 a randomized trial done in the United Kingdom was published, which compared the TVT to Burch colposuspension. The study found that TVT surgery was associated with more intra-operative complications than the Burch procedure, but the latter was associated with more post-operative complications and longer recovery, and the two procedures had comparable cure rates. The authors concluded that TVT showed promise for the treatment of urodynamic SUI because of its minimal invasiveness and rapid recovery time.²²

The “TOMUS” trial was a multi-center, randomized equivalence trial comparing outcomes between retropubic and trans-obturator mid-urethral sling use in women with stress urinary incontinence and was published in the New England Journal of Medicine in 2010. 597 women were randomly assigned to a study group, and 565 completed the twelve-month assessment. The authors found objective treatment success in 80.8% of the patients in the retropubic sling group and in 77.7% of the patients in the trans-obturator sling group. Subjective success was found in 62.2% of the patients in the retropubic sling group and 55.8% of the patients in the trans-obturator sling group. The rate of voiding dysfunction requiring surgery was low—with only 2.7% of the patients receiving retropubic slings and 0% of the patients receiving trans-obturator slings requiring re-operation for voiding dysfunction. More of the patients in the trans-obturator group experienced neurologic symptoms. The differences between the groups with respect to post-operative urge incontinence, satisfaction with the results of the procedure, or quality of life were not statistically significantly different. 2.7% of the patients in the retropubic group experienced mesh exposures classified as serious adverse events, while 0.3% of the patients in the trans-obturator sling group did. None of the retropubic patients experienced new urge incontinence and only one of the trans-obturator patients did. The rate of surgical site infection was 0.7% in both groups. Bladder perforation occurred in 5% of the retropubic patients and

²¹ Thubert T, et al. Bladder injury and success rates following retropubic mid-urethral sling: TVT EXACT vs. TVT. *Eur J Obstet Gynecol Reprod Biol.* 2016 Mar;198:78–83; Aniulienė R, et al., TVT-Exact and midurethral sling (SLING_IUFT) operative procedures: a randomized study. *Open Med (Wars).* 2015 Jun 10;10(1):311-17; Feng S, et al., Three- and twelve-month follow-up outcomes of TVT-EXACT and TVT-ABBREVO for treatment of female stress urinary incontinence: a randomized clinical trial. *World J Urol.* 2018 Mar;36(3):459-65; Sun Y, et al., The Efficiency and Safety of Tension-Free Vaginal Tape (TVT) Abbrevio Procedure Versus TVT Exact in the Normal Weight and Overweight Patients Affected by Stress Urinary Incontinence. *Urology.* 2017 Dec;110:63-69.

²² Ward K and Hilton P on behalf of the United Kingdom and Ireland Tension-free Vaginal Tape Trial Group, Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress urinary incontinence. *BMJ* 2012 Jul;325:1-7.

none of the trans-obturator patients.²³ The authors also published their results at 2 and 5 years after surgery.²⁴

A significant body of high-quality scientific evidence supports the efficacy of mid-urethral slings like the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio. A 2017 Cochrane Review by Ford and colleagues that included 81 trials evaluating 12,113 women noted short-term subjective cure rates from 62-98% for trans-obturator slings and 71-97% for retropubic slings. Short-term objective cure rates in the two types of slings were similar. In the long-term, subjective cure ranged from 43-92% in the trans-obturator sling patients and from 51-88% in the retropubic sling patients. The overall rate of adverse events was low. The authors concluded that mid-urethral sling operations “have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term.” The authors noted that their review “illustrates their positive impact on improving the quality of life of women with SUI.”²⁵

Recurrent incontinence is a potential outcome with any SUI surgery.²⁶ Midurethral slings like the TVT, TVT-O, TVT-Abbrevio, and TVT-Exact devices have been shown to be “highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term.”²⁷ The AUA has noted that “Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries.”²⁸ Intermediate and long-term studies, systematic reviews, meta-analyses, and patient registries support the devices’ safety and efficacy.²⁹

²³ Richter HE, et al., Retropubic versus Transobturator Midurethral Slings for Stress Incontinence. *N Engl J Med* 2010;362(22):2066-76.

²⁴ Albo ME, et al., Treatment Success of Retropubic and Transobturator Mid Urethral Slings at 24 Months. *J Urol*. 2012 Dec;188:2281-87;Kenton K, et al., 5-Year Longitudinal Followup after Retropubic and Transobturator Mid Urethral Slings. *J Urol*. 2015 Jan;193:203-10.

²⁵ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2017 Jul 31;7:CD006375.

²⁶ Kobashi KC, et al., Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. *J Urol*. 2017 Oct;198(4):875-883.

²⁷ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2015 Jul 1;(7):CD006375.

²⁸ AUA Position Statement on the Use of Vaginal mesh for the Surgical Treatment of SUI. October 2013

²⁹ Serati M, et al., Tension-free Vaginal Tape-Obturator for Treatment of Pure Urodynamic Stress Urinary Incontinence: Efficacy and Adverse Effects at 10-year Follow-up. *Eur Urol*. 2017 Apr;71(4):674-79; Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. *Eur Urol* 2014 Jun;65(6):1109-14; Nilsson CG, et al., Falconer C. Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J*. 2013 Aug;24(8):1265-9; Nguyen JN, et al., Perioperative complications and reoperations after incontinence and prolapse surgeries using prosthetic implants. *Obstet Gynecol*. 2012 Mar;119(3):539-46; Tommaselli GA, et al., Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. *Int Urogynecol J*. 2015 Sep;26(9):1253-68; Kuuva N, et al., A nationwide analysis of complications associated with the tension-free vaginal tape (TVT) procedure. *Acta Obstet Gynecol Scand*. 2002 Jan;81(1):72-7; Tamussino KF, et al., Tension-free vaginal tape operation: results of the Austrian registry. *Obstet Gynecol*. 2001 Nov;98(5 Pt 1):732-6; Heinonen P, et al., Tension-free vaginal tape procedure without preoperative

Cox and colleagues published a literature review in 2013, which discussed the published data on the current surgical treatment options for female SUI and whether there was sufficient evidence to suggest a gold standard treatment. Based on their analysis of the literature, they concluded that “a new gold standard first-line surgical treatment for women with SUI is the synthetic midurethral sling inserted through a retropubic or transobturator approach.”³⁰

All surgical treatments of stress urinary incontinence—whether traditional procedures such as the Burch colposuspension or fascial sling procedure or minimally invasive mid-urethral slings such as the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio—involve the same potential complications.³¹

Any incontinence procedure can cause de novo overactive bladder symptoms, but it does not occur with retropubic mid-urethral slings like the TVT and TVT-Exact or with trans-obturator slings like the TVT-O and TVT-Abbrevio significantly more often than it does with other incontinence procedures.³² There is no statistically significant difference between retropubic and trans-obturator slings in the rate of de novo urgency and urgency urinary incontinence.³³

The rate of urinary retention lasting longer than six weeks with retropubic mid-urethral slings like the TVT is only 2.7%—lower than that seen with pubovaginal slings (7.5%) and the Burch

urodynamic examination: long-term outcome. *Int J Urol*. 2012 Nov;19(11):1003-9; Jonsson Funk M, et al., Sling revision/removal for mesh erosion and urinary retention: long-term risk and predictors. *Am J Obstet Gynecol*. 2013 Jan;208(1):73.e1-7; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. *Int Urogynecol J*. 2013 Aug;24(8):1271-8; Welk B, et al., Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence. *JAMA Surg*. 2015 Dec;150(12):1167-75; Angioli R, et al., Tension-Free Vaginal Tape Versus Transobturator Suburethral Tape: Five-Year Follow-up Results of a Prospective, Randomised Trial. *Eur Urol* 2010;58:671–677; Unger CA, et al., Indications and risk factors for midurethral sling revision. *Int Urogynecol J*. 2016 Jan;27(1):117-22; Richter HE, et al., Retropubic versus Transobturator Midurethral Slings for Stress Incontinence. *N Engl J Med* 2010;362:22:2066-76; Serati M, et al., TVT-O for the Treatment of Pure Urodynamic Stress Incontinence: Efficacy, Adverse Effects, and Prognostic Factors at 5-Year Follow-up. *Eur Urol* 2013;63:872–78; Liapis A, et al., Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up. 2010;148:199–201; Groutz A, et al., Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure. *J of Women's Health* 2011;20(10):1525–1528; Cheng D, et al., Tension-free vaginal tape-obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow-up. *Eur J Obstet Gynecol Reprod Biol* 2012;161:228–231; Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. *Eur Urol* 2014 Jun;65(6):1109–14; Angioli R, et al., Tension-Free Vaginal Tape Versus Transobturator Suburethral Tape: Five-Year Follow-up Results of a Prospective, Randomised Trial. *Eur Urol* 2010;58:671–677; Athanasiou S, et al., Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: Why do tapes fail? 2014;25:219–225; Richter HE, et al., Retropubic versus Transobturator Midurethral Slings for Stress Incontinence. *N Engl J Med* 2010;362:22:2066-76.

³⁰ Cox A, et al., Surgical management of female SUI: is there a gold standard? *Nat. Rev. Urol*. 2013;10:78-89.

³¹ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2017 Jul 31;7:CD006375; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;211(1):71.e1-71.e27.

³² Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;211(1):71.e1-71.e27; Kobashi KC, et al., Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. *J Urol*. 2017 Oct;198(4):875-883.

³³ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2015 Jul 1;(7):CD006375.

procedure (7.6%).³⁴ The 2015 and 2017 Cochrane review reported the overall rate of urinary retention with retropubic tapes like the TVT and TVT-Exact as 1.6% and 0.5% with trans-obturator tapes like the TVT-O and TVT-Abbrevio.³⁵ Procedures that do not utilize mesh do not carry a risk of mesh exposure or erosion, but the sutures used in those procedures can become exposed or erode into other structures. The rates of complications seen with retropubic and trans-obturator sling procedures are similar to and often lower than the rates of complications with the traditional procedures. For instance, the Society of Gynecologic Surgeons' Systematic Review Group performed a systematic review and meta-analysis of stress incontinence surgeries and noted the following complication rates, among others, for retropubic and trans-obturator mid-urethral slings compared to the traditional procedures.

	<u>RP MUS</u>	<u>TO MUS</u>	<u>Burch</u>	<u>PVS</u>
Exposure	1.4%	2.2%	0.00%	5.4%
Transfusion	0.40%	0.17%	0.00%	1.9%
Hematoma	0.88%	0.59%	1.4%	2.2%
Dyspareunia	0.00%	0.16%	NR (not reported)	0.99%
Return to O.R. for Erosion	1.9%	2.7%	0.28%	1.6%
Retention lasting > 6 weeks	2.7%	2.4%	7.6%	7.5%
OAB / urgency	6.9%	5.3%	4.3%	8.6%
Wound Infection	0.75%	0.74%	7.0%	2.6%
UTI	11%	4.3%	5.9%	4.2%
Bowel Injury	0.34%	0.00%	NR	3.13%
Ureteral Injury	0.00%	1.22%	0.61%	0.18%
Groin pain	1.5%	6.5%	1.10%	0.34%

³⁴ Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;211(1):71.e1-71.e27.

³⁵ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;(7):CD006375; Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2017 Jul 31;7:CD006375.

	<u>RP MUS</u>	<u>TO MUS</u>	<u>Burch</u>	<u>PVS</u>
Bladder perforation	3.6%	0.70%	2.8%	2.3%
Return to O.R. for urinary retention	1.2%	1.1%	0.00%	3.0%

This table demonstrates that the same complications can occur with any surgical procedure to treat stress urinary incontinence. The SGS systematic review concluded that the evidence supporting the use of mid-urethral slings was of high quality.³⁶

Pain and dyspareunia are reported to occur commonly, with at least 40% of women reporting dyspareunia and/or pelvic pain, and at least 20% reporting chronic dyspareunia and/or pelvic pain.³⁷ Chronic pelvic pain is a common and serious problem among women.³⁸ Rates of dyspareunia and chronic pain with midurethral slings like the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio are very low. A 2015 Cochrane review reported that rates of superficial and deep dyspareunia were low at 24-month follow-up, and sexual function significantly improved from baseline scores.³⁹ The 2014 SGS systematic review noted that the rate of dyspareunia with retropubic midurethral slings like the TVT and TVT-Exact is 0%, and with trans-obturator slings like the TVT-O and TVT-Abbrevio it is 0.16%.⁴⁰ Tommaselli reported in a systematic review and meta-analysis in 2015 that only 13 out of 3,974 retropubic midurethral sling recipients (i.e., 0.3%) and 30 out of 2,432 (i.e., 1.2%) trans-obturator midurethral sling recipients reported persistent or chronic pain.⁴¹ Surgical revision of midurethral slings for dyspareunia or vaginal pain are rare—occurring in 0.2% of patients according to a case-control study involving 3,307 patients by Unger and colleagues.⁴² Furthermore, all surgical treatments of SUI—including pubovaginal slings and the Burch colposuspension—can cause dyspareunia and pain.⁴³

³⁶ Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;211(1):71.e1-71.e27.

³⁷ Jamieson DJ, Steege JF. The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices. *Obstet Gynecol.* 1996 Jan;87(1):55-8.

³⁸ Mathias SD, et al., Chronic Pelvic Pain: Prevalence, Health-Related Quality of Life, and Economic Correlates. *Obstet Gynecol.* 1996 Mar;87(3):321-7.

³⁹ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2015 Jul 1;(7):CD006375.

⁴⁰ Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;211(1):71.e1-71.e27.

⁴¹ Tommaselli GA, et al., Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. *Int Urogynecol J.* 2015;26:1253-68.

⁴² Unger CA, et al., Indications and risk factors for midurethral sling revision. *Int Urogynecol J* (2016) 27:117-122; Gurol-Urganci I, et al., Long-term Rate of Mesh Sling Removal Following Midurethral Mesh Sling Insertion Among Women With Stress Urinary Incontinence. *JAMA.* 2018 Oct 23;320(16):1659-69.

⁴³ Kobashi KC, et al., Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. *J Urol.* 2017 Oct;198(4):875-883.

While scar tissue incorporated into the TVT's pores may contract somewhat during the healing process, the data shows that clinically significant contraction leading to adverse events such as pain or urinary contraction does not occur, as evidenced by the low rates of post-operative pain and urinary retention reported in the literature. Studies have shown that the TVT slings do not contract.⁴⁴

Mesh exposure, erosion, and extrusion is a well-known potential complication of any mesh procedure.⁴⁵ The IFU for the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio devices warn of the potential for erosion and extrusion. The published medical literature discusses the possibility of mesh exposure and erosion, and notes that it occurs very infrequently—in approximately 1-3% of cases.⁴⁶ Surgical revision for mesh exposure or erosion also occurs very infrequently.⁴⁷ Monofilament tapes like the TVT predominate in current clinical practice are noted to have fewer erosions than multifilament mesh tapes.⁴⁸ Type I mesh like the lightweight, macroporous mesh in the TVT has been noted to have “the highest biocompatibility with the least propensity for infection.”⁴⁹

Groin pain and leg pain occur more frequently in connection with trans-obturator mid-urethral sling procedures than they do after retropubic mid-urethral sling procedures. Groin pain has been reported to occur in 0.4% of women undergoing retropubic mid-urethral sling procedures and in 1.6% of women undergoing trans-obturator mid-urethral sling procedures.⁵⁰ However, the groin pain that occurred was usually of short duration and resolved within eight weeks in most cases.⁵¹

⁴⁴ Dietz HP, et al., Does the tension-free vaginal tape stay where you put it? *Am J Obstet Gynecol* 2003;188:950-3; Lo T-S, et al., Ultrasound assessment of mid-urethra tape at three-year follow-up after tension-free vaginal tape procedure; *Urology* 2004;63:671-75; Nilsson CG, et al., Falconer C. Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J.* 2013 Aug;24(8):1265-9.

⁴⁵ Iglesia CB, et al., The Use of Mesh in Gynecologic Surgery. *Int Urogyn J* 1997;8:105-15.

⁴⁶ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2015 Jul 1;(7):CD006375; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;211(1):71.e1-71.e27; Fusco F, et al., Updated Systematic Review and Meta-analysis of the Comparative Data on Colposuspensions, Pubovaginal Slings, and Midurethral Tapes in the Surgical Treatment of Female Stress Urinary Incontinence. *Eur Urol* 2017;72:567-91.

⁴⁷ Nguyen JN, et al., Perioperative Complications and Reoperations After Incontinence and Prolapse Surgeries Using Prosthetic Implants. *Am J Obstet Gynecol* 2012 Mar ;119(3):539-46; Unger CA, et al., Indications and risk factors for midurethral sling revision. *Int Urogynecol J* (2016) 27:117-122; Jonsson Funk M, et al, Sling revision/removal for mesh erosion and urinary retention: long-term risk and predictors. *Am J Obstet Gynecol* 2013;208:73.e1-7.

⁴⁸ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2015 Jul 1;(7):CD006375; Ogah J, et al., Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2009 Oct 7;(4):CD006375.

⁴⁹ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2015 Jul 1;(7):CD006375.

⁵⁰ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2015 Jul 1;(7):CD006375.

⁵¹ Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2015 Jul 1;(7):CD006375.

The Usefulness of the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio Mid-Urethral Sling Devices

I find the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio slings to be safe and effective for the treatment of patients' stress urinary incontinence. It is useful and desirable that the slings are made of Prolene polypropylene—a material that has been extensively used in surgeries for more than 50 years and is known to be well-tolerated by the human body. It is useful and desirable that the slings have been extensively studied, with a significant body of Level 1 evidence supporting the safety and efficacy of the devices. That body of literature—combined with my own experience using the devices—enables me to have comprehensive pre-operative counseling discussions with my patients regarding the potential benefits and risks of the devices. The fact that the devices are made of macroporous, Type I, monofilament mesh is useful and desirable because it allows for excellent tissue ingrowth and a very low rate of infection because the pores are large enough to allow macrophages, fibroblasts, blood vessels, leukocytes, and collagen to transverse the pores.⁵²

Because the slings are minimally invasive, there is less post-operative pain, a shorter post-operative convalescence, and a quicker return to regular activities of daily living than there is with alternative procedures that are more invasive. Mid-urethral sling procedures typically do not require an overnight hospital stay, and the studied and standardized surgical technique has resulted in surgeons throughout the United States and world being able to perform the procedures. As a result, patients' access to treatment is expanded well beyond major metropolitan areas.

The TVT, TVT-Exact, TVT-O, and TVT-Abbrevio devices are made of Prolene polypropylene, a material used in surgery for approximately 50 years, which was approved by the FDA as safe and effective.⁵³ As noted above, the Type I TVT mesh is known for its biocompatibility. The devices can be placed via a small vaginal incision, an easily accessible location just inside the vaginal introitus, which allows short operative times and expeditious post-operative healing. The fact that the slings are implanted at the mid-urethra, and via a small vaginal incision is useful and desirable because it makes the slings minimally invasive. There is no need for a large abdominal incision, and there is no need for harvesting the patient's own fascia lata or rectus fascia, which can result in additional wound complications at the fascial harvest sites and unsightly scars from those incisions. If post-operative urinary retention occurs, it can be treated much more easily after a midurethral sling procedure than it can after retropubic suspensions such as Burch procedures. The devices are implanted in straightforward procedures that can easily be taught and learned, thereby increasing access to the procedure for women suffering from stress urinary incontinence who live outside of metropolitan areas. The TVT, TVT-Exact, TVT-O, and TVT-Abbrevio devices are, in my opinion, safe and effective devices. Their benefits outweigh their risks, and they are not defectively designed.

⁵² Amid PK, Classification of biomaterials and their related complications in abdominal wall hernia surgery. *Hernia* 1997;1:15-21.

⁵³ Librojo Affidavit.

Response to Plaintiff's Experts' Contentions

The published, Level 1, scientific evidence regarding midurethral slings like the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio does not support plaintiffs' experts' contentions that the slings cause a chronic foreign body reaction, are cytotoxic, undergo particle loss, fraying, roping, curling, have inadequate pore size, are heavy weight, or degrade in vivo causing complications. Nor does the published medical literature show a difference in the performance of mid-urethral slings based on the way they are cut.⁵⁴

I have seen no evidence in my practice or in the published literature indicating that particle loss occurs in the body. Even if particle loss did occur, there is no reason to believe that would cause complications, as the particles lost would be the same Prolene material that is recognized as safe and has been used in surgeries for many decades.

I have not observed clinically significant fraying, curling, or roping of the TVT, TVT-Exact, TVT-O, or TVT-Abbrevio devices, nor does the published literature describe that phenomenon in connection with complications.

I have seen no evidence in my clinical experience indicating that the Prolene mesh used in the TVT, TVT-O, TVT-Exact, and TVT-Abbrevio devices degrades in the body. The published literature shows excellent long-term efficacy rates, and I have seen that in my practice as well. If there was degradation occurring, one would expect to see an extreme decline in efficacy over time. What some material scientists have theorized to be evidence of degradation of polypropylene has been found by other experts to be a cracked protein-formaldehyde coating resulting from the formalin fixation process.⁵⁵ The latter is more consistent with my very positive experience using the Prolene mesh devices in my practice and with the positive published data on the use of the devices, as set forth in this report.

While a foreign body reaction is expected with the implantation of any foreign body, the available evidence does not indicate that the Prolene mesh in the TVT, TVT-Exact, and TVT-Abbrevio devices causes clinically significant chronic foreign body reaction. The Prolene mesh in the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio devices has been shown to result in a minimal inflammatory reaction.⁵⁶

Alternative procedures or sling procedures using grafts other than Type I polypropylene mesh like the mesh in the TVT, TVT-Exact, TVT-Abbrevio, and TVT-O are generally not safer or more effective than those devices. Studies show that autologous fascial slings and the Burch procedure are more morbid procedures than synthetic mesh midurethral slings. As noted above, a multi-center RCT comparing autologous fascial sling procedures with the Burch procedure showed that at 24-month follow up, the Burch procedure had an overall success rate of 38% and

⁵⁴ Rusavy Z, et al., Are the same tapes really the same? Ultrasound study of laser-cut and mechanically cut TVT-O post-operative behavior. *Int Urogynecol J* 2017 Nov. doi: 10.1007/s00192-017-23516-z [Epub ahead of print]

⁵⁵ Thames SF, et al., The myth: in vivo degradation of polypropylene-based meshes. *Int Urogynecol J*. 2017 Feb;28(2):285-97.

⁵⁶ Falconer C, et al., Influence of Different Sling Materials on Connective Tissue Metabolism in Stress Urinary Incontinent Women. *Int Urogynecol J*. 2001(Suppl 2):S19-S23.

the fascial sling procedure a success rate of 47%.⁵⁷ The efficacy of the Burch procedure have been reported to be poor at long-term follow up, with only 19% of patients in one study reporting no incontinence episodes at a median of 14 years, with 26% reporting stress incontinence and 42% reporting mixed incontinence.⁵⁸ Richter and colleagues noted that continence rates decreased from 42% to 13% in Burch patients and from 52% to 27% in fascial sling patients during a period of 2 to 7 years post-operatively.⁵⁹ Systematic reviews and meta-analyses, and professional society guidelines show that the complications seen after midurethral sling surgeries are also seen after the Burch procedure or fascial sling procedures.⁶⁰ Cadaveric (allograft) slings or slings made from animal tissue (xenograft) are not widely used. Cadaveric fascia lata slings have a higher failure rate,⁶¹ and been noted to have vaginal erosion rates of up to 23%⁶² It has been noted that efforts to use xenografts or allograft fascia in pubovaginal sling surgery have shown inferior results.⁶³ The use of mesh with larger pores or a lighter weight than the Prolene polypropylene mesh in the TVT, TVT-Exact, TVT-Abbrevio, and TVT-O has not been shown to eliminate or reduce the incidence of the potential complications with the use of those devices.⁶⁴ Ethicon investigated the possibility of utilizing a partially absorbable mesh similar to Ultrapro in a trans-obturator sling, but found that the force required to remove the sheaths was excessive.⁶⁵

Polyvinylidene difluoride ("PVDF") use has been associated with a significant rate of complications including chronic pain, infection, and adhesions. The rate of erosions is not lower than it is with Type I mesh like the Prolene mesh in the TVT, TVT-O, TVT-Abbrevio, and TVT-Exact devices.⁶⁶ There is a paucity of data on slings made of PVDF compared to the extensive body of data regarding the use of Prolene mesh in mid-urethral slings.

⁵⁷ Albo ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence. *N Engl J Med* 2007;356(21):2143-55.

⁵⁸ Kjolhede P, Long-term efficacy of Burch colposuspension: a 14-year follow-up study. *Acta Obstet Gynecol Scand* 2005;84:767-72.

⁵⁹ Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. *J. Urol.* 2012 Aug;188:485-89.

⁶⁰ Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;211(1):71.e1-71.e27; Appell RA et al., Guideline for the Surgical Management of Female Stress Urinary Incontinence: 2009 Update (Rev. 2012); Kobashi KC, et al., Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. *J Urol.* 2017 Oct;198(4):875-883.

⁶¹ Huang YH, et al., High Failure Rate Using Allograft Fascia Lata in Pubovaginal Sling Surgery for Female Stress Urinary Incontinence. *J Urol* 2001;58(6):943-6; Carbone JM, et al., Pubovaginal Sling Using Cadaveric Fascia and Bone Anchors: Disappointing Early Results. *J Urol.* 2001 May;165:1605-11; Soergel TM, et al., Poor Surgical Outcomes after Fascia Lata Allograft Slings. *Int Urogynecol J* 2001;12:247-53; Fitzgerald MP, et al., Medium-term follow-up on use of freeze-dried, irradiated donor fascia for sacrocolpopexy and sling procedures. *Int Urogynecol J* 2004;15:238-42.

⁶² Kammerer-Doak DN, Vaginal Erosion of Cadaveric Fascia Lata following Abdominal Sacrocolpopexy and Suburethral Sling Urethropexy. *Int Urogynecol J* 2002;13:106-09.

⁶³ Kobashi KC, et al., Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. *J Urol.* 2017 Oct;198(4):875-883.

⁶⁴ Okulu E, et al., Use of three types of synthetic mesh material in sling surgery: A prospective randomized clinical trial evaluating effectiveness and complications. *Scan J Urol.* 2013 Jun;47(3):217-24; Milani AL, et al., Trocar-guided mesh repair of vaginal prolapse using partially absorbable mesh: 1 year outcomes. *Am J Obstet Gynecol* 2011;204:74.e1-8.

⁶⁵ R&D Memorandum on PA Mesh Assessments for TVTO-PA. ETH.MESH.09922570-78.

⁶⁶ Klink CD, et al., Comparison of Long-Term Biocompatibility of PVDF and PP Meshes. *J Investigative Surg* 2011;24:292-99; Fortelny RH, et al., Adverse effects of polyvinylidene fluoride-coated polypropylene mesh used for

I have used both laser-cut and mechanically cut slings and have not seen a clinically significant difference in the rate of complications following the use of those slings. I have not seen, for instance, an increased rate of mesh exposure with the use of laser-cut slings, refuting the suggestion by some plaintiffs' experts that laser-cut slings are stiffer, resulting in more mesh exposure. Nor does the published medical literature show a difference in the performance of the mid-urethral slings based on the way they are cut.⁶⁷ Likewise, the published literature from before and during the availability of laser-cut mesh does not show different rates of complications. Ethicon's internal analysis revealed there was no clinical difference between laser-cut mesh and mechanically cut mesh within the range of physiologic forces.⁶⁸

Numerous professional organizations support the safety and efficacy of mid-urethral slings like the TVT, TVT-Exact, TVT-Abbrevio, and TVT-O. The American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) issued a Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence, and the Position Statement was also supported by the American Association of Gynecological Laparoscopists, the American College of Obstetricians and Gynecologists, The National Association for Continence, the International Urogynecological Association, and the Society of Gynecologic Surgeons. The Position Statement notes that "[t]he polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly. With its acknowledged safety and efficacy, it has created an environment for a much larger number of women to have access to treatment. . . . The procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence."⁶⁹ The organizations also noted that the "monofilament polypropylene mesh MUS is the most extensively studied anti-incontinence procedure in history" and that "[a] broad evidence base including high quality scientific papers in medical journals in the US and the world supports the use of the MUS as a treatment for SUI."

The American Urological Association (AUA) and SUFU issued their Guideline for the Surgical Treatment of SUI in 2017 and noted that retropubic mid-urethral slings have a success rate reported to be between 51 and 87%, and that the TVT "is arguably the most widely studied anti-incontinence procedure." The AUA issued its Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence in 2013, noting that the AUA supports

laparoscopic intraperitoneal onlay repair of incisional hernia. *Br J Surg.* 2010 Jul;97(7):1140-5; Göretzlehner U, et al., PVDF as an implant material in urogynaecology. *BIOMaterialien* 2007;8(S1):28-29; Sommer T, et al., DynaMesh in the repair of laparoscopic ventral hernia: a prospective trial. *Hernia* 2013 Oct;17(5):613-8.)

⁶⁷ Rusavy Z, et al., Are the same tapes really the same? Ultrasound study of laser-cut and mechanically cut TVT-O post-operative behavior. *Int Urogynecol J* 2018 Sep;29(9):11335-1340; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;211(1):71.e1-71.e27; Cox A, et al., Surgical management of female SUI: is there a gold standard? *Nat. Rev. Urol.* 2013;10:78-89; Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev.* 2015 Jul 1;(7):CD006375; Novara G, et al., Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. *Eur Urol.* 2010 Aug;58(2):218-38.

⁶⁸ Clinical Expert Report. ETH.MESH.01784823.

⁶⁹ AUGS / SUFU Position Statement – Mesh Midurethral Slings for Stress Urinary Incontinence (Jan. 2014, Updated June 2016, February 2018).

the use of multi-incision monofilament slings for the treatment of SUI in properly selected and counseled patients by surgeons trained to implant them.⁷⁰

The Instructions for Use and Professional Education Materials

I disagree with plaintiffs' experts' contention that the TVT, TVT-Exact, TVT-Abbrevio, or TVT-O Instructions for Use were inadequate. The IFUs set forth how to safely use the devices and list potential complications, including but not limited to the risk of erosion, extrusion, fistula formation, inflammation, de novo detrusor instability, infection, lower urinary tract obstruction, and punctures or lacerations of vessels, nerves, bladder, urethra, or bowel, which may necessitate surgical repair. One must keep in mind that surgeons who are reading the IFUs have completed medical school, an internship, a residency, and sometimes a fellowship. Surgeons read published medical literature regarding their specialty, they talk to colleagues, they attend continuing medical education seminars, and they discuss matters with their colleagues. In other words, there are numerous sources from which surgeons learn of the potential risks and complications associated with a given surgical procedure. Based on my education, training, research, and clinical experience, it is my opinion that the TVT, TVT-Exact, TVT-O, and TVT-Abbrevio IFUs enable surgeons to safely use the devices and do not need to contain additional warnings. In my opinion, it is unnecessary for the IFUs to contain information regarding the frequency or severity of potential complications because the frequency of complications is published in medical literature, varies from surgeon to surgeon, and surgeons know that any complication that occurs can be of varying levels of severity.

Surgeons have extensive bodies of knowledge gained from many sources, regarding the surgical treatment of SUI and the risks associated with it.⁷¹ The risks of pelvic surgery have been reported extensively in the peer-reviewed literature for many decades.⁷²

⁷⁰ AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence (2013).

⁷¹ ACGME Program Requirements for Graduate Medical Education in Female Pelvic Medicine and Reconstructive Surgery, sec. IV.A.5.b).(3); ABOG & ABU Guide to Learning in Female Pelvic Medicine and Reconstructive Surgery 2012.

⁷² Iglesia CB, et al., The use of mesh in gynecologic surgery. *Int Urogynecol J Pelvic Floor Dysfunct.* 1997; 8:105-15; Williams TH and TeLinde RW, The Sling Operation for Urinary Incontinence Using Mersilene Ribbon. *Obstet Gynecol* 1962; 19:241-245; Morgan JE. A sling operation, using Marlex polypropylene mesh, for treatment of recurrent stress incontinence. *Am J Obstet Gynecol.* 1970; 106:369-77; Amias AG. Sexual life after gynaecological operations—II. *Br Med J.* 1975; 2:680-1; Stanton SL, et al., Silastic sling for urethral sphincter incompetence in women. *Br J Obstet Gynaecol.* 1985 Jul;92(7):747-50; Weber AM, et al., Sexual function and vaginal anatomy in women before and after surgery for pelvic organ prolapse and urinary incontinence. *Am J Obstet Gynecol.* 2000; 182:1610-5; Chaliha C and Stanton SL. Complications of surgery for genuine stress incontinence. *Br J Obstet Gynaecol.* 1999; 106:1238-45; Haase P and Skibsted L. Influence of operations for stress incontinence and/or genital descensus on sexual life. *Acta Obstet Gynecol Scand* 1988; 67:659-61; Francis WJ and Jeffcoate TN. Dyspareunia following vaginal operations. *J Obstet Gynaecol Br Commonw* 1961; 68:1-10; Mainprize TC, Drutz HP. The Marshall-Marchetti-Krantz procedure: a critical review. *Obstet Gynecol Surv.* 1988 Dec;43(12):724-9; Stanton SL, Stress incontinence: why and how operations work. *Clin Obstet Gynaecol.* 1985; 12:369-77, *Urol Clin North Am.* 1985; 12:279-84; Alcalay M, et al., Burch colposuspension: a 10-20 year follow up. *Br J Obstet Gynaecol.* 1995 Sep;102(9):740-5; Handa VL, et al., Banked human fascia lata for the suburethral sling procedure: a preliminary report. *Obstet Gynecol.* 1996; 88:1045-9; Moir JC, The gauze-hammock operation. (A modified Aldridge sling procedure). *J Obstet Gynaecol Br Commonw.* 1968; 75:1-9; Galloway NT, et al., The complications of colposuspension. *Br J Urol.* 1987; 60:122-4; Fitzgerald MP, et al., Failure of allograft suburethral slings. *BJU Int.*

Ethicon also produced the Surgeon's Resource Monograph after a 17-surgeon panel meeting in June of 2000, which set forth expert opinions on the use of the TVT device with respect to patient selection, surgical techniques with respect to patient positioning, administration of anesthesia, surgical incisions, and device placement. It also discussed post-operative care, contraindications, adverse reactions, and potential complications including vaginal bleeding, retropubic hematoma, vaginal perforation, difficulty with needle placement, bladder perforations, voiding dysfunction, urethral injury, urethral erosion, mesh protrusion, vascular injury, bowel perforations, de novo urge incontinence, infection of the mesh, UTI, and failure of the device.⁷³ Documents like the IFU, Ethicon's professional education materials, and the Surgeon's Resource Monograph were helpful to surgeons and unavailable for procedures such as the Burch colposuspension, MMK, or fascial sling procedures.

Conclusion

The TVT, TVT-Exact, TVT-O, and TVT-Abbrevio mid-urethral slings are safe and effective, and their benefits outweigh their risks. The mid-urethral sling has revolutionized the treatment of stress urinary incontinence, providing a durable treatment option that is less invasive than the

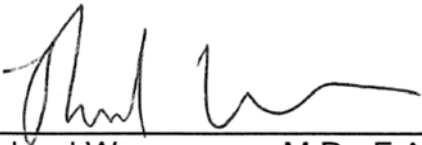
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⁷³ Surgeon's Resource Monograph. ETH.MESH.00658177-98.

traditional procedures that came before it. The opinions set forth in this report are based on my analysis of the published literature regarding the treatment of stress urinary incontinence, the deposition testimony provided to me, the materials cited in this report and those included on my reliance list, and on my education, training, and clinical experience treating gynecologic disorders. I reserve the right to supplement my opinions if I receive additional information. I hold the opinions set forth in this report to a reasonable degree of medical and scientific certainty.

I have not testified as an expert witness in a trial or deposition in the preceding four years.

Dated: 3/21/19

A handwritten signature in black ink, appearing to read 'Richard Wasserman', written over a horizontal line.

Richard Wasserman, M.D., F.A.C.O.G.